~~MMP2-12 Inhibitors~~ 10/613788

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TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS	4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	8	JAN 30	Saved answer limit increased
NEWS	9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	14	FEB 28	TOXCENTER reloaded with enhancements
NEWS	15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	16	MAR 01	INSPEC reloaded and enhanced
NEWS	17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	18	MAR 08	X.25 communication option no longer available after June 2006
NEWS	19	MAR 22	EMBASE is now updated on a daily basis
NEWS	20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS	21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS	22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS	23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS	24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS	25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

MMP-13 inhibitors

FILE 'HOME' ENTERED AT 12:06:05 ON 13 APR 2006

=> file medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 12:06:18 ON 13 APR 2006

FILE LAST UPDATED: 12 APR 2006 (20060412/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s corticosteroids
L1    .    30823 CORTICOSTEROIDS

=> s corticosteroid?
L2        48819 CORTICOSTEROID?

=> s corticosteroi?
L3        48824 CORTICOSTEROI?

=> s HVGD or host-versus-graft
             12 HVGD
         157574 HOST
         210879 VERSUS
         143254 GRAFT
            282 HOST-VERSUS-GRAFT
                  (HOST(W)VERSUS(W)GRAFT)
L4          285 HVGD OR HOST-VERSUS-GRAFT

=> s transplant(w)rejection
          64238 TRANSPLANT
          58516 REJECTION
L5         1830 TRANSPLANT(W)REJECTION

=> s L3 and (L4 or L5)
```

MMP-13 inhibitors

L6 56 L3 AND (L4 OR L5)

=> s L6 and topical
55292 TOPICAL
L7 3 L6 AND TOPICAL

=> d L7 1-3 ti abs bib

L7 ANSWER 1 OF 3 MEDLINE on STN
TI Immunomodulatory therapy in ophthalmology - is there a place for **topical** application?.
AB **Topical corticosteroids**, although effective in the treatment of ocular immune-mediated diseases, are well known for their ocular side-effects. Not surprisingly, a variety of alternative immunomodulatory agents have been tested for **topical** use including cyclosporin A (CsA), mycophenolate mofetil (MMF), tacrolimus (FK506), rapamycin (sirolimus) and leflunomide. Local application bears the possibility to avoid the severe side-effects of systemic therapy. The effect of **topical** therapy is naturally restricted to local immune response mechanisms, such as antigen presentation by Langerhans and dendritic cells. Moreover, many immunomodulatory agents (e.g. CsA) are lipophilic and thus have low water solubility and penetrate insufficiently intra-ocularly, often being stored in the lipophilic corneal epithelial barrier. Therefore, the therapeutical success is limited for intra-ocular immune-mediated diseases like anterior uveitis. However, a multitude of strategies have been introduced to circumvent these problems including complexing substances such as cyclodextrins (CDs) and liposomes. In the prevention and treatment of **transplant rejection** after keratoplasty, many attempts to introduce **topical** immunomodulatory therapy have failed; on the other hand, further therapeutic options not primarily expected are being evaluated today such as treatment of severe keratoconjunctivitis sicca. In our own studies, we investigated the pharmacokinetics of **topical** treatment with different agents including MMF and evaluated the efficacy of **topical** treatment in animal models for uveitis and keratoplasty. Taken together, **topical** immunomodulatory therapy will not replace systemic therapy but further treatment options can be expected.
AN 2004591965 MEDLINE
DN PubMed ID: 15564752
TI Immunomodulatory therapy in ophthalmology - is there a place for **topical** application?.
AU Bertelmann Eckart; Pleyer Uwe
CS Augenklinik Charite - Universitatsmedizin Berlin, Campus Virchow Klinikum, Berlin, Deutschland.. eckart.bertelmann@charite.de
SO Ophthalmologica. Journal international d'ophtalmologie. International journal of ophthalmology. Zeitschrift fur Augenheilkunde, (2004 Nov-Dec) Vol. 218, No. 6, pp. 359-67. Ref: 71
Journal code: 0054655. ISSN: 0030-3755.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200501
ED Entered STN: 20041130
Last Updated on STN: 20050112
Entered Medline: 20050111

L7 ANSWER 2 OF 3 MEDLINE on STN
TI Therapeutic potential of macrolide immunosuppressants in dermatology.
AB Dermatologists are frequently presented with inflammatory dermatoses that

are responsive to treatment with immunomodulating drugs. **Corticosteroids**, particularly when applied topically, have been the mainstay of treatment in the past. Their undoubted efficacy, however, has been undermined by problems with repeated use including tachyphylaxis and side effects such as skin atrophy and hypertension. Macrolide immunosuppressive drugs, originally used for prophylaxis of organ **transplant rejection**, have been shown to be effective in the treatment of inflammatory dermatoses. The original drugs used in dermatology in this class have their own limitations including poor absorption when used topically and their distinct side-effect profiles. A search for other immunosuppressive macrolide antibiotics has led to the development of new agents, which have enhanced profiles for the treatment of skin disease. This review discusses the main dermatoses that may be targeted by this class of drugs and summarises the **topical** and systemic macrolides either currently in use, in clinical trials or preclinical development.

AN 2004107513 MEDLINE
DN PubMed ID: 14996647
TI Therapeutic potential of macrolide immunosuppressants in dermatology.
AU Marsland Alexander M; Griffiths Christopher E M
CS Konishi-MUSC Institute for Inflammation Research, Medical University of South Carolina, Charleston, SC 29425, USA.
SO Expert opinion on investigational drugs, (2004 Feb) Vol. 13, No. 2, pp. 125-37. Ref: 202
Journal code: 9434197. ISSN: 1354-3784.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200412
ED Entered STN: 20040305
Last Updated on STN: 20041220
Entered Medline: 20041216

L7 ANSWER 3 OF 3 MEDLINE on STN
TI Subepithelial infiltrates: a probable sign of corneal **transplant rejection**.
AB A previously undescribed slit-lamp manifestation of a probable corneal **transplant rejection** reaction was found in 22 patients among 145 who underwent penetrating keratoplasty during a two-year period. The reaction consisted of subepithelial infiltrates that were located only in the donor tissue; were without associated conjunctivitis; and that occurred six weeks to 21 months postoperatively, either alone or in association with epithelial and/or endothelial rejection; and that responded well to **topical corticosteroid** treatment. In one case, the subepithelial infiltrates preceded a severe endothelial rejection by only a few days. The lesions are a warning that all is not well and that **corticosteroid** therapy should be instituted or increased.
AN 79061577 MEDLINE
DN PubMed ID: 363109
TI Subepithelial infiltrates: a probable sign of corneal **transplant rejection**.
AU Krachmer J H; Alldredge O C
SO Archives of ophthalmology, (1978 Dec) Vol. 96, No. 12, pp. 2234-7.
Journal code: 7706534. ISSN: 0003-9950.
CY United States
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals

MMP-13 inhibitors

EM 197901
ED Entered STN: 19900314
    Last Updated on STN: 19900314
    Entered Medline: 19790126

=> s mometsasone and (L4 or L5)
            0 MOMETSASONE
L8   0 MOMETSASONE AND (L4 OR L5)

=> file registry
COST IN U.S. DOLLARS   SINCE FILE ENTRY   TOTAL SESSION
FULL ESTIMATED COST   2.61   2.82

FILE 'REGISTRY' ENTERED AT 12:09:25 ON 13 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 11 APR 2006 HIGHEST RN 880129-32-8
DICTIONARY FILE UPDATES: 11 APR 2006 HIGHEST RN 880129-32-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> s mometasone
L9   5 MOMETASONE

=> s mometasone/cn
L10   1 MOMETASONE/CN

=> sel l10
E1 THROUGH E3 ASSIGNED

=> file medline

MMP-13 inhibitors

COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION
FULL ESTIMATED COST | 10.29 | 13.11

FILE 'MEDLINE' ENTERED AT 12:09:45 ON 13 APR 2006

FILE LAST UPDATED: 12 APR 2006 (20060412/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s E1-E3
           306 "(+)-MOMETASONE"/BI
                 ("MOMETASONE"/BI)
           306 MOMETASONE/BI
             0 105102-22-5/BI
L11        306 ("(+)-MOMETASONE"/BI OR MOMETASONE/BI OR 105102-22-5/BI)

=> s L11 and (L4 or L5)
L12          0 L11 AND (L4 OR L5)

=> s L11 and transplan?
        388869 TRANSPLAN?
L13          2 L11 AND TRANSPLAN?

=> d L13 1-2 ti abs bib

L13  ANSWER 1 OF 2     MEDLINE on STN
TI   Pressure alopecia in living donors for liver transplantation.
AN   2004065184     MEDLINE
DN   PubMed ID: 14766700
TI   Pressure alopecia in living donors for liver transplantation.
AU   Tomioka Toshiya; Hayashida Masakazu; Hanaoka Kazuo
SO   Canadian journal of anaesthesia = Journal canadien d'anesthesie, (2004
     Feb) Vol. 51, No. 2, pp. 186-7.
     Journal code: 8701709. ISSN: 0832-610X.
CY   Canada
DT   Letter
LA   English
FS   Priority Journals
EM   200408
ED   Entered STN: 20040210
     Last Updated on STN: 20040811
     Entered Medline: 20040810

L13  ANSWER 2 OF 2     MEDLINE on STN
```

MMP-13 inhibitors

TI A local lymph node assay to analyse immunosuppressive effects of topically applied drugs.
AB Topical glucocorticosteroids represent the mainstay of antiinflammatory therapy in the treatment of inflammatory skin diseases. Their clinical use, however, is limited by local and systemic side-effects. Thus, in dermatopharmacology there is a large demand for alternative non-steroidal antiinflammatories. Other than **transplantation** models, most of the frequently used in vivo test systems for assessment of drug-induced immunosuppression measure changes in inflammatory skin responses by means of skin erythema and edema after challenge of sensitized animals. The aim of this study was to develop an alternative mouse model to detect and analyse immunosuppressive effects of topically applied drugs. On the basis of a modified local lymph node assay, we analysed effects of topical hydrocortisone, dexamethasone, **mometasone** furoate and FK506 (tacrolimus) during the induction phase of contact hypersensitivity. On 4 consecutive days, NMRI mice were treated on the dorsal surfaces of both ears with increasing concentrations of test compound. During the last 3 days, the mice received in addition the contact sensitizer, oxazolone (1%). On day 5, draining auricular lymph nodes were removed in order to assess lymph node cell counts and perform flow cytometric analysis of lymph node cell subpopulations (CD4+/CD25+, Ia+/CD69+, Ia+/B220+). All test compounds proved to exert significant immunosuppressive effects after topical application, but showed differences in their immunomodulatory potential. In conclusion, the local lymph node assay serves as an appropriate model to characterize immunosuppressive effects of topically applied drugs by measuring immunologically relevant end-points.
AN 97306099 MEDLINE
DN PubMed ID: 9163567
TI A local lymph node assay to analyse immunosuppressive effects of topically applied drugs.
AU Homey B; Schuppe H C; Assmann T; Vohr H W; Lauerma A I; Ruzicka T; Lehmann P
CS Department of Dermatology, Heinrich Heine University, Dusseldorf, Germany.
SO European journal of pharmacology, (1997 May 1) Vol. 325, No. 2-3, pp. 199-207.
Journal code: 1254354. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199708
ED Entered STN: 19970813
Last Updated on STN: 19970813
Entered Medline: 19970804

=> s L6 and py>2000
3024827 PY>2000
(PY>20009999)
L14 15 L6 AND PY>2000

=> s l6 not L14
L15 41 L6 NOT L14

=> dup rem L15
PROCESSING COMPLETED FOR L15
L16 41 DUP REM L15 (0 DUPLICATES REMOVED)

=> d L16 1-41 ti

L16 ANSWER 1 OF 41 MEDLINE on STN
TI Economics of the antithymocyte globulins Thymoglobulin and Atgam in the

treatment of acute renal **transplant rejection**.

L16 ANSWER 2 OF 41 MEDLINE on STN
TI Pharmacokinetic monitoring of mycophenolate mofetil in kidney transplanted patients.

L16 ANSWER 3 OF 41 MEDLINE on STN
TI Evidence that apoptosis of activated T cells occurs in spontaneous tolerance of liver allografts and is blocked by manipulations which break tolerance.

L16 ANSWER 4 OF 41 MEDLINE on STN
TI Sirolimus (rapamycin)-based therapy in human renal transplantation: similar efficacy and different toxicity compared with cyclosporine. Sirolimus European Renal Transplant Study Group.

L16 ANSWER 5 OF 41 MEDLINE on STN
TI Liver granulomatosis is not an exceptional cause of hypercalcemia with hypoparathyroidism in dialysis patients.

L16 ANSWER 6 OF 41 MEDLINE on STN
TI Overview of transplantation immunology and the pharmacotherapy of adult solid organ transplant recipients: focus on immunosuppression.

L16 ANSWER 7 OF 41 MEDLINE on STN
TI Hyperlipidemia in renal transplant recipients treated with sirolimus (rapamycin).

L16 ANSWER 8 OF 41 MEDLINE on STN
TI Proposed consensus for definitions and endpoints for clinical trials of acute kidney **transplant rejection**.

L16 ANSWER 9 OF 41 MEDLINE on STN
TI Extracorporeal photochemotherapy: a treatment for organ graft rejection.

L16 ANSWER 10 OF 41 MEDLINE on STN
TI Sirolimus, a new, potent immunosuppressive agent.

L16 ANSWER 11 OF 41 MEDLINE on STN
TI Prevention of **transplant rejection**: current treatment guidelines and future developments.

L16 ANSWER 12 OF 41 MEDLINE on STN
TI [Mycophenolate mofetil, a new immunosuppressive agent. Is pharmacokinetic monitoring justified?].
Le mycophenolate mofetil, un nouvel immunosuppresseur. Une surveillance pharmacocinetique est-elle justifiee?.

L16 ANSWER 13 OF 41 MEDLINE on STN
TI Preliminary risk-benefit assessment of mycophenolate mofetil in **transplant rejection**.

L16 ANSWER 14 OF 41 MEDLINE on STN
TI Mycophenolate mofetil in renal allograft recipients: a pooled efficacy analysis of three randomized, double-blind, clinical studies in prevention of rejection. The International Mycophenolate Mofetil Renal Transplant Study Groups.

L16 ANSWER 15 OF 41 MEDLINE on STN
TI Mycophenolate mofetil for the transplanted kidney?.

L16 ANSWER 16 OF 41 MEDLINE on STN

MMP-13 inhibitors

TI Muromonab CD3: a reappraisal of its pharmacology and use as prophylaxis of solid organ **transplant rejection**.

L16 ANSWER 17 OF 41 MEDLINE on STN
TI Mycophenolate mofetil for the treatment of refractory, acute, cellular renal **transplant rejection**. The Mycophenolate Mofetil Renal Refractory Rejection Study Group.

L16 ANSWER 18 OF 41 MEDLINE on STN
TI Perforin expression in peripheral blood lymphocytes in rejecting and tolerant kidney transplant recipients.

L16 ANSWER 19 OF 41 MEDLINE on STN
TI Pathogenesis of pulmonary aspergillosis. Granulocytopenia versus cyclosporine and methylprednisolone-induced immunosuppression.

L16 ANSWER 20 OF 41 MEDLINE on STN
TI [Muromonab CD3 (Orthoclone OKT3) for the prophylaxis of heart allograft rejection. Hemodynamics and respiratory tolerance].
Le muromonab CD3 (Orthoclone OKT3) en prophylaxie de rejet d'allogreffe cardiaque. Tolerance hemodynamique et respiratoire.

L16 ANSWER 21 OF 41 MEDLINE on STN
TI Value of serum soluble tumour necrosis factor concentrations in the diagnosis and prognosis of renal graft rejection.

L16 ANSWER 22 OF 41 MEDLINE on STN
TI Uses, adverse effects of abuse of **corticosteroids**. Part I.

L16 ANSWER 23 OF 41 MEDLINE on STN
TI Mechanisms of endothelial cell injury in vasculitis.

L16 ANSWER 24 OF 41 MEDLINE on STN
TI Alterations in renal interleukin-1 production during kidney **transplant rejection** in the rat. The effects of high-dose methylprednisolone.

L16 ANSWER 25 OF 41 MEDLINE on STN
TI Cyclosporin. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in immunoregulatory disorders.

L16 ANSWER 26 OF 41 MEDLINE on STN
TI Leukocyte adhesion molecules: potential targets for therapeutic intervention in kidney diseases.

L16 ANSWER 27 OF 41 MEDLINE on STN
TI [Orthotopic liver transplantation (first clinical experience)].
Ortotopicheskaia transplantatsiia pecheni (pervyi klinicheskii opyt).

L16 ANSWER 28 OF 41 MEDLINE on STN
TI Successful treatment of heart **transplant rejection** with photopheresis.

L16 ANSWER 29 OF 41 MEDLINE on STN
TI Photopheresis versus **corticosteroids** in the therapy of heart **transplant rejection**. Preliminary clinical report.

L16 ANSWER 30 OF 41 MEDLINE on STN
TI Mechanism, pathophysiology, diagnosis, and management of renal **transplant rejection**.

L16 ANSWER 31 OF 41 MEDLINE on STN

MMP-13 inhibitors

TI Muromonab CD3. A review of its pharmacology and therapeutic potential.

L16 ANSWER 32 OF 41 MEDLINE on STN
TI Uremic optic neuropathy.

L16 ANSWER 33 OF 41 MEDLINE on STN
TI A prospective study on the use of monoclonal anti-T3-cell antibody (OKT3) to treat steroid-resistant liver **transplant rejection**.

L16 ANSWER 34 OF 41 MEDLINE on STN
TI Celestone phosphate injection high dose: treatment of septic shock and impending **transplant rejection**.

L16 ANSWER 35 OF 41 MEDLINE on STN
TI Acute and long-term complications of **corticosteroid** pulse therapy.

L16 ANSWER 36 OF 41 MEDLINE on STN
TI Cyclosporine in treatment of **corticosteroid**-resistant episodes of rejection.

L16 ANSWER 37 OF 41 MEDLINE on STN
TI Improved outcome following renal transplantation with reduction in the immunosuppression therapy for rejection episodes.

L16 ANSWER 38 OF 41 MEDLINE on STN
TI Opportunistic pneumonia: a clinicopathological study of five cases caused by an unidentified acid-fast bacterium.

L16 ANSWER 39 OF 41 MEDLINE on STN
TI Joint effusions after kidney transplantation.

L16 ANSWER 40 OF 41 MEDLINE on STN
TI Subepithelial infiltrates: a probable sign of corneal **transplant rejection**.

L16 ANSWER 41 OF 41 MEDLINE on STN
TI Effects of glucocorticoids on carbohydrate metabolism.

```
=> s L16 and (transplant(w)rejection)/ti
L17          41 S L16
         25489 TRANSPLANT/TI
         12813 REJECTION/TI
           600 (TRANSPLANT(W)REJECTION)/TI
L18          13 L17 AND (TRANSPLANT(W)REJECTION)/TI

=> d L18 ti abs bib
```

L18 ANSWER 1 OF 13 MEDLINE on STN
TI Economics of the antithymocyte globulins Thymoglobulin and Atgam in the treatment of acute renal **transplant rejection**.
AB OBJECTIVE: To evaluate the economic implications for transplant centres, Medicare and society of treatment of **corticosteroid**-resistant Banff Grades I, II and III acute kidney **transplant rejection** with the antithymocyte globulins Thymoglobulin or Atgam. DESIGN AND SETTING: This was a cost analysis of a randomised double-blind multicentre clinical trial comparing the safety and efficacy of Thymoglobulin and Atgam that was performed at 25 centres in the US in 1994 to 1996. PATIENTS AND PARTICIPANTS: The study enrolled 163 patients, 82 in the Thymoglobulin arm and 81 in the Atgam arm. METHODS: Estimates of the cost of care from the initiation of rejection therapy to 90 days

post-therapy were derived from various publicly available sources and applied to patient-specific clinical events documented in the clinical trial. Patients received either intravenous Thymoglobulin (1.5 mg/kg/day) for an average of 10 days or intravenous Atgam (15 mg/kg/day) for an average of 9.7 days. RESULTS: On average, Thymoglobulin provided significant cost savings compared with Atgam from the perspective of society [$US5977 (1996 values); 95% confidence interval (CI) $US3719 to $US8254], Medicare ($US4967; 95% CI $US3256 to $US6678) and the transplant centre ($US3087; 95% CI $US1512 to $US4667). The overall advantage attributable to Thymoglobulin was primarily due to savings from fewer recurrent rejection treatments and less frequent return to dialysis. CONCLUSIONS: Treatment of acute renal **transplant rejection** with Thymoglobulin is a cost saving strategy when compared with treatment with Atgam.

AN 2001004278 MEDLINE
DN PubMed ID: 10947303
TI Economics of the antithymocyte globulins Thymoglobulin and Atgam in the treatment of acute renal **transplant rejection**.
AU Schnitzler M A; Woodward R S; Lowell J A; Amir L; Schroeder T J; Singer G G; Brennan D C
CS Pharmaco-Economic Transplant Research, Washington University, St Louis, Missouri, USA.. schnitz@wueconc.wustl.edu
SO PharmacoEconomics, (2000 Mar) Vol. 17, No. 3, pp. 287-93.
Journal code: 9212404. ISSN: 1170-7690.
CY New Zealand
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Health Technology
EM 200006
ED Entered STN: 20010223
Last Updated on STN: 20020125
Entered Medline: 20000630

=> d L18 2-13 ti abs bib

L18 ANSWER 2 OF 13 MEDLINE on STN
TI Proposed consensus for definitions and endpoints for clinical trials of acute kidney **transplant rejection**.
AB Progress in transplantation therapeutics requires validation from multicenter trials in which enrollment criteria and endpoint definitions have been standardized. A database of acute rejection was established from 19 North American, European, and Australian transplant centers and included parameters on rejection diagnosis and treatment of 50 consecutive rejection episodes from each center. Patient demographics, induction and maintenance immunosuppressive therapies, antirejection agents (drug, dose, duration), clinical signs (decrease in urine volume, presence of fever of > or =38.5 degrees C), serum creatinine concentration (nadir, at rejection, daily during antirejection therapy to 15 days, and days 30, 90, 180, and 365 after rejection date), rejection biopsy findings, morbidity, recurrence of rejection, and renal function at 1 year were recorded for 953 rejection episodes. From these data, three definitions were proposed. Acute rejection was defined as an immunologic process resulting in a serum creatinine increase of > or =0.4 mg/dL, with or without clinical signs, and should include a biopsy confirmation that has been standardized to the Banff criteria. **Corticosteroid**-resistant rejection was defined as a rejection episode in which a minimum of 250 to 1000 mg of methylprednisolone administered as initial therapy fails to result in stabilization or reduction of the serum creatinine after 3 days of **corticosteroid** treatment. Successful response to therapy was

defined as a serum creatinine level < or =110% of the serum creatinine on the day of the rejection diagnosis and a return of the serum creatinine to or below the rejection creatinine level by 5 days of therapy with maintenance of this response for a minimum of 30 days. The work represented in the Efficacy Endpoints Database provides a step toward improving definitions in clinical trials. Continuity in clinical trial design should lead to improvements in evaluation of outcomes and, thereby have an effect on clinical practice.

AN 1998293624 MEDLINE
DN PubMed ID: 9631863
TI Proposed consensus for definitions and endpoints for clinical trials of acute kidney **transplant rejection**.
AU Guttmann R D; Soulillou J P; Moore L W; First M R; Gaber A O; Pouletty P; Schroeder T J
CS Centre for Clinical Immunobiology & Transplantation, McGill University, Montreal, Canada.. rdg@zoo.net
SO American journal of kidney diseases : the official journal of the National Kidney Foundation, (1998 Jun) Vol. 31, No. 6 Suppl 1, pp. S40-6. Journal code: 8110075. ISSN: 0272-6386.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199807
ED Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980702

L18 ANSWER 3 OF 13 MEDLINE on STN
TI Prevention of **transplant rejection**: current treatment guidelines and future developments.
AB In the past 2 decades, progressive improvements in the results of organ transplantation as a therapeutic strategy for patients with end-stage organ disease have been achieved due to greater insight into the immunobiology of graft rejection and better measures for surgical and medical management. It is now known that T cells play a central role in the specific immune response of acute allograft rejection. Strategies to prevent T cell activation or effector function are thus all potentially useful for immunosuppression. Standard immunosuppressive therapy in renal transplantation consists of baseline therapy to prevent rejection and short courses of high-dose **corticosteroids** or monoclonal or polyclonal antibodies as treatment of ongoing rejection episodes. Triple-drug therapy with the combination of cyclosporin, **corticosteroids** and azathioprine is now the most frequently used immunosuppressive drug regimen in cadaveric kidney recipients. The continuing search for more selective and specific agents has become, in the past decade, one of the priorities for transplant medicine. Some of these compounds are now entering routine clinical practice: among them are tacrolimus (which has a mechanism of action similar to that of cyclosporin), mycophenolate mofetil and mizoribine (which selectively inhibit the enzyme inosine monophosphate dehydrogenase, the rate-limiting enzyme for de novo purine synthesis during cell division), and sirolimus (rapamycin) [which acts on and inhibits kinase homologues required for cell-cycle progression in response to growth factors, like interleukin-2 (IL-2)]. Other new pharmacological strategies and innovative approaches to organ transplantation are also under development. Application of this technology will offer enormous potential not only for the investigation of mechanisms and mediators of graft rejection but also for therapeutic intervention.

AN 97479879 MEDLINE
DN PubMed ID: 9339960
TI Prevention of **transplant rejection**: current treatment

guidelines and future developments.
AU Perico N; Remuzzi G
CS Department of Transplant Immunology and Innovative Antirejection Therapies, Ospedali Riuniti, Istituto di Ricerche Farmacologiche Mario Negri, Bergamo, Italy.
SO Drugs, (1997 Oct) Vol. 54, No. 4, pp. 533-70. Ref: 320
Journal code: 7600076. ISSN: 0012-6667.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199711
ED Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971113

L18 ANSWER 4 OF 13 MEDLINE on STN
TI Preliminary risk-benefit assessment of mycophenolate mofetil in **transplant rejection**.
AB Mycophenolate mofetil (the morpholinoethyl ester of mycophenolic acid) inhibits de novo purine synthesis via the inhibition of inosine monophosphate dehydrogenase. Its selective lymphocyte antiproliferative effects involve both T and B cells, preventing antibody formation. Mycophenolate mofetil has immuno-suppressive effects alone, but is used most commonly in combination with other immunosuppressants. Mycophenolate mofetil, in combination with cyclosporin and **corticosteroids**, has been studied in large, randomised clinical trials involving nearly 1500 renal allograft transplant recipients. These trials demonstrated that mycophenolate mofetil is significantly more effective in reducing treatment failure and acute rejection episodes than placebo or azathioprine. Additionally, mycophenolate mofetil may be able to reduce the occurrence of chronic rejection. Mycophenolate mofetil is relatively well tolerated. The most common adverse effect reported is gastrointestinal intolerance; haematological aberrations have also been noted. The reversible cytostatic action of mycophenolate mofetil allows for dose adjustment or discontinuation, preventing serious toxicity or an overly suppressed immune system. Cytomegalovirus tissue invasive disease and the development of malignancies are concerns that merit evaluation in long term follow-up studies. Mycophenolate mofetil does not cause the adverse effects typically associated with other commercially available immunosuppressant medications such as nephrotoxicity, hepatotoxicity, hypertension, nervous system disturbances, electrolyte abnormalities, skin disorders, hyperglycaemia, hyperuricaemia, hypercholesterolaemia, lipid disorders and structural bone loss. Based on preliminary information, a positive benefit-risk ratio has been demonstrated with the use of mycophenolate mofetil in the prophylaxis of rejection in cadaveric renal allograft transplantation. Data from studies in other types of organ transplants are promising, but are too limited to draw clear conclusions. Long term follow-up studies are required to confirm these observations. Although mycophenolate mofetil is expensive, the beneficial effects on the reduction of rejection, treatment failure and related expenses suggest that it is most likely to be cost effective.
AN 97431100 MEDLINE
DN PubMed ID: 9285199
TI Preliminary risk-benefit assessment of mycophenolate mofetil in **transplant rejection**.
AU Simmons W D; Rayhill S C; Sollinger H W
CS Department of Pharmacy, University of Wisconsin Hospital and Clinics, Madison, USA.. WD.SIMMONS@HOSP.WISC.EDU
SO Drug safety : an international journal of medical toxicology and drug experience, (1997 Aug) Vol. 17, No. 2, pp. 75-92. Ref: 68

MMP-13 inhibitors

Journal code: 9002928. ISSN: 0114-5916.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971105
Last Updated on STN: 19971105
Entered Medline: 19971022

L18 ANSWER 5 OF 13 MEDLINE on STN
TI Muromonab CD3: a reappraisal of its pharmacology and use as prophylaxis of solid organ **transplant rejection**.
AB The murine monoclonal antibody muromonab CD3 (OKT3) is directed against the CD3 antigen on peripheral human T cells and effectively blocks all T cell function. Prophylaxis with muromonab CD3 (5mg intravenously once daily for 10 to 14 days) as induction therapy together with **corticosteroids**, azathioprine and delayed cyclosporin (sequential therapy) optimises early graft function by delaying the potentially nephrotoxic and hepatotoxic effects of cyclosporin until graft function is established. Although clinical data are limited (by inconsistencies in trial design and trial size), prophylactic muromonab CD3-based sequential therapy is significantly more effective than standard triple therapy in the prophylaxis of allograft rejection in renal and hepatic, but not cardiac, transplant recipients. Benefits are particularly notable in patients with delayed graft function. No significant between-treatment differences in patient survival have been observed. The overall efficacy of muromonab CD3- and polyclonal-based prophylactic regimens appears to be similar, although results vary between investigators and confirmation is needed. An anti-interleukin-2 monoclonal antibody-based prophylactic regimen improved graft and patient survival compared with muromonab CD3-based prophylaxis in hepatic transplant recipients. Antimuromonab CD3 antibodies may develop; however, muromonab CD3 may be successfully reused in patients with low titres. Preliminary pharmacoeconomic data suggest that mean drug costs are greater with quadruple immunosuppressive regimens containing muromonab CD3, antithymocyte globulin (ATG) or antilymphocyte globulin (ALG) than with triple therapy. Drug costs with prophylactic muromonab CD3-based regimens were similar or greater than those with polyclonal-based protocols. The first doses of muromonab CD3 are associated with the 'cytokine-release syndrome'. More severe first-dose events include aseptic meningitis, intragraft thromboses, seizures and potentially fatal pulmonary oedema. The incidence and/or severity of cytomegalovirus infection with prophylactic muromonab CD3 based immunosuppression is similar to or greater than that with triple therapy and ATG- or ALG-based regimens. However, the risk of infection and also the observed increase in lymphoproliferative disorders appears to be related to the degree of immunosuppression rather than to the drug itself Thus, sequential muromonab CD3-based therapy is more effective than standard triple therapy (in renal and hepatic transplant recipients) and appears to be similar to that of polyclonal-based regimens in the prophylaxis of **transplant rejection**. Although the routine use of prophylactic muromonab CD3 in low-risk patients with primary graft function does not appear to be justified, prophylactic muromonab CD3-based therapy has a role in patients at high risk of rejection.
AN 97014718 MEDLINE
DN PubMed ID: 8861551
TI Muromonab CD3: a reappraisal of its pharmacology and use as prophylaxis of solid organ **transplant rejection**.
AU Wilde M I; Goa K L
CS Adis International Limited, Auckland, New Zealand.

MMP-13 inhibitors

SO Drugs, (1996 May) Vol. 51, No. 5, pp. 865-94. Ref: 214
Journal code: 7600076. ISSN: 0012-6667.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970602
Last Updated on STN: 19970602
Entered Medline: 19970522

L18 ANSWER 6 OF 13 MEDLINE on STN
TI Mycophenolate mofetil for the treatment of refractory, acute, cellular renal **transplant rejection**. The Mycophenolate Mofetil Renal Refractory Rejection Study Group.
AB In a 6-month open label, randomized, multicenter trial, we compared the efficacy and safety of mycophenolate mofetil (MMF) with high dose intravenous steroids (IVS) for the treatment of refractory, acute cellular rejection in recipients of first or second cadaveric or living-donor renal allografts. A total of 150 patients were enrolled and randomized in a 1-to-1 ratio to receive oral MMF 1.5 g twice daily (n=77) or i.v. methylprednisolone 5 mg/kg for 5 days (n= 73), tapered over the subsequent 5 days to 20 mg/day or the baseline dose of steroid given on the day before the diagnosis of rejection. Patients in both groups generally received cyclosporine and maintenance doses of **corticosteroids** throughout the study period. The IVS group (but not the MMF group) was generally maintained on azathioprine. The primary efficacy variable was graft and patient survival at 6 months. Graft loss and death were reduced by 45% in the MMF treatment group; 19 patients (26.0%) in the IVS group experienced graft loss or died, compared with 11 patients (14.3%) in the MMF group (P=0.081, sequential probability ratio test analysis). In the IVS group, 64.4% of patients experienced either subsequent biopsy proven rejection, presumptive rejection (presumed rejection clinically diagnosed but not biopsy proven and treated with a full course of immunosuppressive therapy), or treatment failure (premature termination for any reason, including death, graft loss, or an adverse event) compared with 39.0% in the MMF group (P=0.001, Cochran-Mantel-Haenszel [CMH] general association test). One or more full courses of immunosuppressive treatment for subsequent rejection episodes were administered to 35.6% of patients in the IVS group and 24.7% of patients in the MMF group. The number of patients who received full courses of **corticosteroids** for subsequent episodes of rejection was equal in the 2 groups, but the number of patients who received full courses of antilymphocyte therapy was more than twice as great in the IVS group (n = 18) compared with the MMF group (n=8). Adverse events were reported in 74.6% of patients who received IVS and in 93.5% of patients who received MMF. A cerebral lymphoma developed in 1 patient in each group, and a lymphoproliferative disorder developed in 2 patients in the MMF group; in 1 of these patients, the lymphoproliferative disorder was subsequently determined to be present before study entry. Opportunistic infections occurred in 35% of patients in each treatment group.
AN 96179046 MEDLINE
DN PubMed ID: 8607174
TI Mycophenolate mofetil for the treatment of refractory, acute, cellular renal **transplant rejection**. The Mycophenolate Mofetil Renal Refractory Rejection Study Group.
AU Anonymous
SO Transplantation, (1996 Mar 15) Vol. 61, No. 5, pp. 722-9.
Journal code: 0132144. ISSN: 0041-1337.
CY United States
DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199605
ED Entered STN: 19960531
Last Updated on STN: 19960531
Entered Medline: 19960523

L18 ANSWER 7 OF 13 MEDLINE on STN
TI Alterations in renal interleukin-1 production during kidney **transplant rejection** in the rat. The effects of high-dose methylprednisolone.
AB To characterize the role of interleukin-1 in renal allograft rejection, we examined the temporal relationship of IL-1 production to changes in renal function and histology in a rat kidney transplantation model. In rat renal allografts, both glomerular filtration rate and renal plasma flow (RPF) fell progressively from days 4 through 6 following transplantation. The reduction in allograft function was accompanied by histologic changes consistent with rejection and enhanced steady-state levels of IL-1 beta mRNA measured by Northern blot. This increase in IL-1 beta mRNA levels was associated with a forty-fold increase in IL-1 bioactivity in eluates of kidney allografts compared with isografts. In rejecting allografts, these changes also coincided with increased production of thromboxane B2 (TxB2) by the graft. To attempt to modify IL-1 production in the transplanted kidney, a separate group of animals with renal allografts were treated with 80 mg/kg/day of methylprednisolone for 6 days. GFR in MP-treated animals was significantly preserved compared with vehicle-treated animals. However, similar histologic manifestations of rejection were found in both groups. Although IL-1 beta mRNA levels in the kidney were not changed with MP treatment, renal IL-1 bioactivity was reduced four-fold in animals that received MP compared with controls. Thus, IL-1 beta gene expression and IL-1 protein production are stimulated in rejecting kidney transplants. MP administration improves allograft function and inhibits IL-1 production, apparently at a post-transcriptional level. We hypothesize that overproduction of IL-1 during kidney **transplant rejection** may promote allograft dysfunction and injury. Some of the beneficial effects of **corticosteroids** in acute rejection may be mediated through inhibition of IL-1 release within the allograft.
AN 94069730 MEDLINE
DN PubMed ID: 8249118
TI Alterations in renal interleukin-1 production during kidney **transplant rejection** in the rat. The effects of high-dose methylprednisolone.
AU Mannon R B; Sundar S K; Sanfilippo F P; Coffman T M
CS Department of Medicine, Duke University, Durham, North Carolina.
NC PO1-DK38103 (NIDDK)
SO Transplantation, (1993 Nov) Vol. 56, No. 5, pp. 1157-62.
Journal code: 0132144. ISSN: 0041-1337.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199312
ED Entered STN: 19940201
Last Updated on STN: 19940201
Entered Medline: 19931230

L18 ANSWER 8 OF 13 MEDLINE on STN
TI Photopheresis versus **corticosteroids** in the therapy of heart

transplant rejection. Preliminary clinical report.

AB BACKGROUND. Photopheresis is a technique in which reinfusion of mononuclear cells exposed to UV-A light ex vivo after in vivo treatment with 8-methoxypsoralen initiates host-immunosuppressive responses. METHODS AND RESULTS. To determine if photopheresis safely reverses International Society for Heart and Lung Transplantation (ISHLT) rejection grades 2, 3A, and 3B without hemodynamic compromise, 16 heart transplant patients with ISHLT rejection grades 2, 3A, and 3B were randomized to photopheresis or **corticosteroid** therapy. The average number of mononuclear cells treated with each photopheresis procedure was 9.8 +/- 9.1 x 10(9) (mean +/- SD). Photopheresis and **corticosteroids** reversed eight of nine and seven of seven episodes of rejection, respectively. The median time from initiation of treatment to rejection reversal was 25 days (range, 6-67 days) in the photopheresis group and 17 days (range, 8-33 days) in the **corticosteroid** group. Hemodynamics were normal before either treatment and did not change after reversal of rejection. No adverse reactions occurred with photopheresis, and all patients in either treatment group are alive. CONCLUSIONS. These preliminary, short-term results in prospectively randomized patients indicate that photopheresis may be as effective as **corticosteroids** for treating ISHLT rejection grades 2, 3A, and 3B. The apparently low toxicity and potential efficacy of photopheresis warrant further analysis of its role in the prevention and treatment of heart **transplant rejection**.

AN 93047149 MEDLINE

DN PubMed ID: 1424007

TI Photopheresis versus **corticosteroids** in the therapy of heart **transplant rejection**. Preliminary clinical report.

AU Costanzo-Nordin M R; Hubbell E A; O'Sullivan E J; Johnson M R; Mullen G M; Heroux A L; Kao W G; McManus B M; Pifarre R; Robinson J A

CS Department of Medicine, Loyola University of Chicago, Maywood.

SO Circulation, (1992 Nov) Vol. 86, No. 5 Suppl, pp. II242-50. Journal code: 0147763. ISSN: 0009-7322.

CY United States

DT (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199212

ED Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921202

L18 ANSWER 9 OF 13 MEDLINE on STN

TI Successful treatment of heart **transplant rejection** with photopheresis.

AB Photopheresis is a potential therapy for rejection in which reinfusion of mononuclear cells exposed to ultraviolet-A light ex vivo, after treatment with 8-methoxypsoralen in vivo, initiates host immune responses that specifically inhibit the cytotoxicity of the photomodulated mononuclear cells. Between May 1990 and January 1991, 7 heart transplant (HT) patients (age 42.2 +/- 16.7 [mean +/- SD] years) on triple immunosuppression (cyclosporine, **corticosteroids**, and azathioprine) had 9 episodes of non-hemodynamically compromising moderate rejection that were treated with photopheresis. These episodes of rejection occurred at an average of 114.4 +/- 180.5 (range 8-575) days after HT. After oral administration the mean serum level of 8-methoxypsoralen achieved was 129.0 +/- 72.4 ng/ml. An average of 10.4 +/- 9.6 x 10(9) mononuclear cells were treated with each photopheresis procedure. Photopheresis was performed twice when less than 5 x 10(9) mononuclear cells had been treated with the first procedure. Of 9

rejection episodes treated with photopheresis, 5 required 1 procedure and 4 required 2 procedures. Photopheresis was used to treat a single episode of rejection in 5 pts. and 2 separate rejection episodes in 2 additional pts. Eight of 9 episodes of rejection were successfully reversed by photopheresis as assessed by endomyocardial biopsy (EMB) performed 7 days after treatment. Immunohistochemical analysis of EMB samples revealed that postphotopheresis cell counts for T cells, B cells, and macrophages were reduced compared to pretreatment values and correlated with the histopathologic resolution of rejection. Hemodynamics were normal prephotopheresis and remained unchanged at the time when the postphotopheresis EMB showed no evidence rejection No adverse effects have been observed with photopheresis. Over a follow-up period of 5.3 +/- 4.0 months, rejection and infection rates/pt./follow-up months were 0.3 +/- 0.4 and 0.04 +/- 0.07, respectively. The preliminary, short term results of this pilot study indicate that photopheresis may be efficacious in the treatment of moderate rejection in hemodynamically stable HT patients and thus may be an alternative to **corticosteroid** pulses.

AN 92229843 MEDLINE
DN PubMed ID: 1566346
TI Successful treatment of heart **transplant rejection** with photopheresis.
AU Costanzo-Nordin M R; Hubbell E A; O'Sullivan E J; Johnson M R; Mullen G M; Heroux A L; Kao W G; McManus B M; Pifarre R; Robinson J A
CS Department of Medicine, Loyola University of Chicago, Maywood, Illinois 60153.
SO Transplantation, (1992 Apr) Vol. 53, No. 4, pp. 808-15.
Journal code: 0132144. ISSN: 0041-1337.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199205
ED Entered STN: 19920607
Last Updated on STN: 19920607
Entered Medline: 19920519

L18 ANSWER 10 OF 13 MEDLINE on STN
TI Mechanism, pathophysiology, diagnosis, and management of renal **transplant rejection**.
AB In recent years, there has been a steady progress in basic research (immunogenetics and cellular immunology) that helped us in understanding the mechanisms underlying allograft rejection. Several laboratory tests were developed, and the results were shown to correlate with clinical rejection. However, most of these studies have not found a place in clinical practice because of their nonspecificity, lack of sensitivity, time lag, added expense, and inconvenience. The commonly employed diagnostic tests (i.e., renal transplant ultrasound and 131I hippuran scintigram) are helpful in differentiating rejection from other causes of graft malfunction. The specific renal parenchymal disease, such as acute or chronic rejection or de novo or recurrent glomerular disease, contributing to graft malfunction can only be diagnosed by renal histopathologic study. Because hyperacute and accelerated acute rejections are irreversible and necessitate graft nephrectomy, measures should be taken to prevent this problem. High-dose **corticosteroids** still remain the mainstay of therapy for acute cellular rejection. In the case of steroid-resistant rejections, treatment with ALG or OKT3 appears promising. As there is no effective therapy for chronic allograft rejection, usual measures of delaying the progression of chronic renal failure should be employed, and patients should be advised to return to maintenance dialysis before they develop uremic symptoms. If current experiments demonstrating selective immunosuppression with monoclonal antibodies are found successful in human

trials, one can expect further improvement in the outcome of renal transplantation.
AN 90309450 MEDLINE
DN PubMed ID: 2114510
TI Mechanism, pathophysiology, diagnosis, and management of renal **transplant rejection**.
AU Rao K V
CS University of Minnesota Medical School, Minneapolis.
SO The Medical clinics of North America, (1990 Jul) Vol. 74, No. 4, pp. 1039-57. Ref: 96
Journal code: 2985236R. ISSN: 0025-7125.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199008
ED Entered STN: 19900921
Last Updated on STN: 19900921
Entered Medline: 19900813

L18 ANSWER 11 OF 13 MEDLINE on STN
TI A prospective study on the use of monoclonal anti-T3-cell antibody (OKT3) to treat steroid-resistant liver **transplant rejection**.
AB Conventional treatment of acute liver allograft rejection has included high doses of **corticosteroids** and antithymocyte globulin. Urgent retransplantation was the only option for patients who failed to respond. We report our initial experience with the use of monoclonal anti-T3-cell antibody (OKT3) in 25 patients with acute hepatic allograft rejection that was resistant to steroid and/or antithymocyte globulin therapy. Twenty-four of 25 patients had a response to OKT3, which was complete in 14 and partial in ten. With a mean follow-up of 8.2 months, allograft salvage has been 80% and patient survival 88%; two patients underwent successful retransplantation. Side effects have been mild and well tolerated. Repeated rejection has occurred in 40% of patients, but these episodes have responded to steroid therapy. We conclude that OKT3 is well tolerated and highly effective in reversing severe episodes of acute hepatic allograft rejection that is resistant to high-dose steroid therapy.
AN 88023318 MEDLINE
DN PubMed ID: 3310962
TI A prospective study on the use of monoclonal anti-T3-cell antibody (OKT3) to treat steroid-resistant liver **transplant rejection**.
AU Colonna J O 2nd; Goldstein L I; Brems J J; Vargas J H; Brill J E; Berquist W J; Hiatt J R; Busuttil R W
CS Department of Surgery, UCLA School of Medicine.
SO Archives of surgery (Chicago, Ill. : 1960), (1987 Oct) Vol. 122, No. 10, pp. 1120-3.
Journal code: 9716528. ISSN: 0004-0010.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198710
ED Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19871029

L18 ANSWER 12 OF 13 MEDLINE on STN
TI Celestone phosphate injection high dose: treatment of septic shock and impending **transplant rejection**.
AB Celestone Phosphate Injection was administered as an intravenous bolus to

twenty patients, eighteen with septic shock and two with impending acute renal **transplant rejection**. Within 4 hours following the diagnosis of septic shock, adjunctive **corticosteroid** therapy in a dosage ranging from 2.88-3.11 mg/kg was given every 4 hours. The two patients with impending acute renal **transplant rejection** were dosed every 24 hours. Intravenous fluids, ventilatory assistance, antimicrobial agents, vasoactive agents, diuretics, digitalis and antipyretics were among the concomitant therapies. Among measurements monitored during the study, vital signs, arterial blood gases, central venous pressure, complete blood count, blood chemistry, electrocardiograms and chest radiographs indicated improvement in each patient's condition by the end of therapy. Rapid clinical improvement occurred within 4-8 hours for patients with septic shock and within 48 hours for patients with kidney transplants. Two to three doses of medication were required. Complete reversal of shock was achieved in eighteen (100%) patients with septic shock; both (100%) renal transplant patients experienced reversal of impending rejection. Tolerance was good and no adverse experiences were reported.

AN 84286345 MEDLINE
DN PubMed ID: 6381171
TI Celestone phosphate injection high dose: treatment of septic shock and impending **transplant rejection**.
AU Carreno C A
SO The Journal of international medical research, (1984) Vol. 12, No. 4, pp. 266-70.
Journal code: 0346411. ISSN: 0300-0605.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198410
ED Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19841019

L18 ANSWER 13 OF 13 MEDLINE on STN
TI Subepithelial infiltrates: a probable sign of corneal **transplant rejection**.
AB A previously undescribed slit-lamp manifestation of a probable corneal **transplant rejection** reaction was found in 22 patients among 145 who underwent penetrating keratoplasty during a two-year period. The reaction consisted of subepithelial infiltrates that were located only in the donor tissue; were without associated conjunctivitis; and that occurred six weeks to 21 months postoperatively, either alone or in association with epithelial and/or endothelial rejection; and that responded well to topical **corticosteroid** treatment. In one case, the subepithelial infiltrates preceded a severe endothelial rejection by only a few days. The lesions are a warning that all is not well and that **corticosteroid** therapy should be instituted or increased.
AN 79061577 MEDLINE
DN PubMed ID: 363109
TI Subepithelial infiltrates: a probable sign of corneal **transplant rejection**.
AU Krachmer J H; Alldredge O C
SO Archives of ophthalmology, (1978 Dec) Vol. 96, No. 12, pp. 2234-7.
Journal code: 7706534. ISSN: 0003-9950.
CY United States
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals

MMP-13 inhibitors

EM 197901
ED Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19790126

MMP-13 inhibitors 10/613788

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NEWS	4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	6	JAN 17	Pre-1988 INPI data added to MARPAT
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NEWS	11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	14	FEB 28	TOXCENTER reloaded with enhancements
NEWS	15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	16	MAR 01	INSPEC reloaded and enhanced
NEWS	17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	18	MAR 08	X.25 communication option no longer available after June 2006
NEWS	19	MAR 22	EMBASE is now updated on a daily basis
NEWS	20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS	21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS	22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS	23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS	24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS	25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

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CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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MMP-13 inhibitors

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FULL ESTIMATED COST	0.21	0.21

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See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

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```
=> s corticosteroid and liver
         23517 CORTICOSTEROID
        642600 LIVER
L1        1296 CORTICOSTEROID AND LIVER

=> s L1 and transplant
         64238 TRANSPLANT
L2          85 L1 AND TRANSPLANT

=> s L1 and transplant(w)rejection
         64238 TRANSPLANT
         58516 REJECTION
          1830 TRANSPLANT(W)REJECTION
L3           3 L1 AND TRANSPLANT(W)REJECTION

=> d L3 ti abs bib

L3   ANSWER 1 OF 3     MEDLINE on STN
TI   Biologics in the treatment of transplant rejection and
     ischemia/reperfusion injury: new applications for TNFalpha inhibitors?.
AB   Tumor necrosis factor (TNF)-alpha inhibitors have proven efficacy in
     various autoimmune diseases such as Crohn disease, rheumatoid arthritis,
     psoriasis, and ankylosing spondylitis.  Indeed, some TNFalpha inhibitors
     have already been approved for the management of the inflammatory
```

manifestations associated with Crohn disease and rheumatoid arthritis. These agents are increasingly used for treatment of **corticosteroid** -resistant graft-versus-host disease after bone marrow transplantation, and case reports have documented their efficacy in treating **corticosteroid**- and muromonab-resistant rejection after intestinal transplantation. Thus, the potential role of TNFalpha inhibitors in transplantation of other vascularized solid organs is worthy of investigation. Experimental evidence indicates that TNFalpha plays a key role in mediating ischemia/reperfusion (IR) injury after **liver**, kidney, intestine, heart, lung, and pancreas transplantation. TNFalpha was also identified as a marker cytokine during organ rejection. Single-center studies evaluating the role of TNFalpha inhibitors in kidney transplantation have been initiated but the results are not yet available. TNFalpha is known to be a contributing factor in kidney allograft rejection, and may have value in predicting the onset of steroid-resistant acute rejection after **liver** transplantation. Experimental and preliminary clinical data have shown that circulating levels of TNFalpha are increased during cardiac graft rejection, and indicate that TNFalpha plays a role in the pathogenesis of acute cardiac allograft rejection. Anti-TNFalpha therapy was shown to prolong cardiac allograft survival when used alone or in combination with other drugs. TNFalpha genotype has been strongly associated with mortality in humans due to acute cell-mediated heart **transplant rejection**. In addition, there is evidence for a genetic predisposition toward acute rejection after kidney and simultaneous kidney-pancreas transplantation. TNFalpha inhibition has been used successfully as part of an induction therapy for pancreatic islet cell transplantation. Apart from IR injury and acute rejection after lung transplantation, TNFalpha was also found to be involved in the pathoimmunology of obliterative bronchiolitis. In conclusion, a substantial body of experimental evidence and preliminary clinical data suggest that TNFalpha inhibitors may play an important role in solid-organ transplantation, both in the amelioration of IR injury and in the treatment and prevention of acute rejection. Pharmacodynamic monitoring and pharmacogenetic screening may help to identify patients most likely to benefit from TNFalpha blockade. Randomized controlled trials in patients undergoing solid-organ transplantation are needed to further elucidate the clinical value of TNFalpha inhibition.

AN 2005461453 MEDLINE
DN PubMed ID: 16128605
TI Biologics in the treatment of **transplant rejection** and ischemia/reperfusion injury: new applications for TNFalpha inhibitors?.
AU Pascher Andreas; Klupp Jochen
CS Department of Visceral and Transplantation Surgery, Charite-Universitaetsmedizin Berlin, Campus Virchow Klinikum, Berlin, Germany.. andreas.pascher@charite.de
SO BioDrugs : clinical immunotherapeutics, biopharmaceuticals and gene therapy, (2005) Vol. 19, No. 4, pp. 211-31. Ref: 261
Journal code: 9705305. ISSN: 1173-8804.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200603
ED Entered STN: 20050831
Last Updated on STN: 20060328
Entered Medline: 20060327

=> d L3 2-3 ti abs bib

L3 ANSWER 2 OF 3 MEDLINE on STN

MMP-13 inhibitors

TI Conversion from cyclosporin to tacrolimus in paediatric **liver** transplant recipients.

AB Substitution of cyclosporin with tacrolimus should be considered for paediatric **liver** transplant recipients with cyclosporin-associated complications such as hypertension, gum hyperplasia, hirsutism, gynaecomastia and growth retardation, as well as recurrent or refractory acute rejection, chronic duct injury or chronic rejection. Continued experience with well tolerated drug administration and careful monitoring during drug substitution has limited drug toxicity associated with tacrolimus to a level comparable to or less than that associated with cyclosporin. Successful outcome with long term graft salvage has been reported in up to 80% of patients converted to tacrolimus because of acute rejection and 50% of patients converted because of chronic rejection. Nearly all children converted because of cyclosporin-related complications have a successful outcome. Additional benefits of conversion to tacrolimus include improvement in growth and resolution of hypertension, hirsutism and cushingoid facies. Complete **corticosteroid** withdrawal is possible in up to 78% of children post-conversion. Long term outcome in these patients may be optimised by conversion to tacrolimus at an early stage of acute or chronic **transplant rejection** in order to minimise the cumulative amount of immunosuppression. Avoidance of cyclosporin-related toxicity and minimisation of **corticosteroid** therapy may further improve patient compliance to drug therapy.

AN 2001635464 MEDLINE

DN PubMed ID: 11688597

TI Conversion from cyclosporin to tacrolimus in paediatric **liver** transplant recipients.

AU Mazariegos G V; Salzedas A A; Jain A; Reyes J

CS Thomas E. Starzl Transplantation Institute, Children's Hospital of Pittsburgh, University of Pittsburgh Medical Center, PA 15213, USA.. mazarieg@pitt.edu

SO Paediatric drugs, (2001) Vol. 3, No. 9, pp. 661-72. Ref: 48
Journal code: 100883685. ISSN: 1174-5878.

CY New Zealand

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LA English

FS Priority Journals

EM 200203

ED Entered STN: 20011105
Last Updated on STN: 20020320
Entered Medline: 20020319

L3 ANSWER 3 OF 3 MEDLINE on STN

TI Evidence that apoptosis of activated T cells occurs in spontaneous tolerance of **liver** allografts and is blocked by manipulations which break tolerance.

AB BACKGROUND: Fully allogeneic **liver** grafts from piebald virol glaxo to dark agouti rats are spontaneously tolerated, whereas kidney transplants between these strains are rejected. **Liver** tolerance is broken by donor irradiation or peritransplant **corticosteroid** treatment of recipient rats, both of which interfere with the activation of recipient cells. METHODS: In this study we used a combination of immunohistochemical staining, reverse transcription-polymerase chain reaction, and terminal deoxynucleotide transferase-mediated dUTP nick end labeling and Annexin-V apoptosis assays to compare donor cell migration, cytokine profiles, and leukocyte apoptosis in grafts and lymphoid organs from tolerant **liver** and rejecting kidney recipients. We then examined the effect on apoptosis of treatments which abrogate **liver** tolerance. RESULTS: **Liver** transplantation in this tolerant strain combination is accompanied by rapid migration of many

passenger leukocytes to the recipient spleen and lymph node, concurrent with a marked but transient increase in the amount of mRNA for the cytokines interleukin-2 and interferon-gamma. Apoptotic cells appear promptly in the spleen, their numbers reaching a peak 2 days earlier than has been previously shown for the graft infiltrate. Both CD4+ and CD8+ T cells undergo apoptosis and apoptotic cells are most concentrated among CD25+ T cells. In contrast, renal **transplant rejection** is associated with limited donor cell migration to lymphoid tissues and significantly less up-regulation of interleukin-2 and interferon-gamma in the spleen. Few apoptotic cells are detected in spleen or graft infiltrate during rejection, whereas apoptotic renal tubular and glomerular cells are found from day 5. Either recipient steroid treatment or donor irradiation significantly reduced the number of apoptotic cells in **liver** graft infiltrates and recipient spleen. CONCLUSIONS: Taken together, these findings suggest that a mechanism akin to activation-induced cell death, with apoptosis of alloreactive recipient cells may be responsible for the induction of spontaneous **liver** transplant tolerance.

AN 2000076064 MEDLINE
DN PubMed ID: 10609951
TI Evidence that apoptosis of activated T cells occurs in spontaneous tolerance of **liver** allografts and is blocked by manipulations which break tolerance.
AU Sharland A; Yan Y; Wang C; Bowen D G; Sun J; Sheil A G; McCaughan G W; Bishop G A
CS AW Morrow Liver Immunobiology Laboratory, Centenary Institute, Royal Prince Alfred Hospital and University of Sydney, NSW, Australia.
SO Transplantation, (1999 Dec 15) Vol. 68, No. 11, pp. 1736-45.
Journal code: 0132144. ISSN: 0041-1337.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106

```
=> s l1 and (HVGD or host(w)versus(w)graft)
            12 HVGD
        157574 HOST
        210879 VERSUS
        143254 GRAFT
           282 HOST(W)VERSUS(W)GRAFT
L4           0 L1 AND (HVGD OR HOST(W)VERSUS(W)GRAFT)

=> s corticosteroid and (HVGD or host(w)versus(w)graft)
         23517 CORTICOSTEROID
            12 HVGD
        157574 HOST
        210879 VERSUS
        143254 GRAFT
           282 HOST(W)VERSUS(W)GRAFT
L5           1 CORTICOSTEROID AND (HVGD OR HOST(W)VERSUS(W)GRAFT)

=> l l5 ti abs bbi
L IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).
```

MMP-13 inhibitors

=> d l5 ti abs bib

L5 ANSWER 1 OF 1 MEDLINE on STN
TI Engraftment syndrome following hematopoietic stem cell transplantation.
AB During neutrophil recovery following hematopoietic stem cell transplantation, a constellation of symptoms and signs including fever, erythrodermatous skin rash, and noncardiogenic pulmonary edema often occur. These clinical findings have usually been referred to as engraftment syndrome, or, reflecting the manifestations of increased capillary permeability, capillary leak syndrome. While described most often following autologous stem cell transplantation, a similar clinical syndrome has been observed followed allogeneic stem cell transplantation. Distinction from graft-versus-host disease in the allogeneic setting however, has been difficult. Recent experience with non-myeloablative conditioning for stem cell transplantation, however, reveals that an engraftment syndrome independent of GVHD may occur. In some cases, this engraftment syndrome may be a manifestation of a **host-versus-graft** reaction (graft rejection). While cellular and cytokine interactions are believed to be responsible for these clinical findings, a distinct effector cell population and cytokine profile have not been defined. Engraftment syndromes are likely associated with an increased transplant-related mortality, mostly from pulmonary and associated multi-organ failure. **Corticosteroid** therapy is often dramatically effective for engraftment syndrome, particularly for the treatment of the pulmonary manifestations. A proposal for a more uniform definition of engraftment syndrome has been developed in order to allow for a reproducible method of reporting of this complication and for evaluating prophylactic and therapeutic strategies.
AN 2002013666 MEDLINE
DN PubMed ID: 11436099
TI Engraftment syndrome following hematopoietic stem cell transplantation.
AU Spitzer T R
CS Department of Medicine, Massachusetts General Hospital, Boston, MA 02114, USA.
SO Bone marrow transplantation, (2001 May) Vol. 27, No. 9, pp. 893-8. Ref: 43
Journal code: 8702459. ISSN: 0268-3369.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20020121
Last Updated on STN: 20020121
Entered Medline: 20011221

=> d L2 1-40 ti

L2 ANSWER 1 OF 85 MEDLINE on STN
TI Population pharmacokinetics of tacrolimus in whole blood and plasma in asian **liver transplant** patients.

L2 ANSWER 2 OF 85 MEDLINE on STN
TI Effect of **corticosteroid** therapy on outcomes in biliary atresia after Kasai portoenterostomy.

L2 ANSWER 3 OF 85 MEDLINE on STN
TI Rapid multifocal chondrolysis after **liver** transplantation in four patients.

MMP-13 inhibitors

L2 ANSWER 4 OF 85 MEDLINE on STN
TI The clinical course of ulcerative colitis after orthotopic **liver** transplantation for primary sclerosing cholangitis: further appraisal of immunosuppression post transplantation.

L2 ANSWER 5 OF 85 MEDLINE on STN
TI Biologics in the treatment of **transplant** rejection and ischemia/reperfusion injury: new applications for TNFalpha inhibitors?.

L2 ANSWER 6 OF 85 MEDLINE on STN
TI Combined treatment with pegylated interferon (alpha-2b) and ribavirin in the acute phase of hepatitis C virus recurrence after **liver** transplantation.

L2 ANSWER 7 OF 85 MEDLINE on STN
TI New-onset diabetes after **liver** transplantation: from pathogenesis to management.

L2 ANSWER 8 OF 85 MEDLINE on STN
TI Risk stratification and targeted antifungal prophylaxis for prevention of aspergillosis and other invasive mold infections after **liver** transplantation.

L2 ANSWER 9 OF 85 MEDLINE on STN
TI A comparison of tacrolimus and cyclosporine in **liver** transplantation: effects on renal function and cardiovascular risk status.

L2 ANSWER 10 OF 85 MEDLINE on STN
TI Pulse cyclophosphamide for **corticosteroid**-refractory graft-versus-host disease.

L2 ANSWER 11 OF 85 MEDLINE on STN
TI **Corticosteroid**-free immunosuppression with tacrolimus following induction with daclizumab: a large randomized clinical study.

L2 ANSWER 12 OF 85 MEDLINE on STN
TI A case of laryngeal posttransplantation lymphoproliferative disease.

L2 ANSWER 13 OF 85 MEDLINE on STN
TI Tacrolimus and steroids versus ciclosporin microemulsion, steroids, and azathioprine in children undergoing **liver** transplantation: randomised European multicentre trial.

L2 ANSWER 14 OF 85 MEDLINE on STN
TI Time-related clinical determinants of long-term tacrolimus pharmacokinetics in combination therapy with mycophenolic acid and corticosteroids: a prospective study in one hundred de novo renal **transplant** recipients.

L2 ANSWER 15 OF 85 MEDLINE on STN
TI Overlap syndrome of primary biliary cirrhosis and autoimmune hepatitis with unusual initial presentation as fulminant hepatic failure.

L2 ANSWER 16 OF 85 MEDLINE on STN
TI Clinical pharmacokinetics and pharmacodynamics of tacrolimus in solid organ transplantation.

L2 ANSWER 17 OF 85 MEDLINE on STN
TI Alterations of CYP3A4 and P-glycoprotein activity in vivo with time in renal graft recipients.

L2 ANSWER 18 OF 85 MEDLINE on STN

MMP-13 inhibitors

TI Interleukin-2 receptor antibody (basiliximab) for immunosuppressive induction therapy after **liver** transplantation: a protocol with early elimination of steroids and reduction of tacrolimus dosage.

L2 ANSWER 19 OF 85 MEDLINE on STN
TI Immunosuppression: practice and trends.

L2 ANSWER 20 OF 85 MEDLINE on STN
TI Low incidence of cytomegalovirus disease in **liver transplant** recipients receiving sirolimus primary immunosuppression with 3-day **corticosteroid** taper.

L2 ANSWER 21 OF 85 MEDLINE on STN
TI [Evaluation of drug therapy knowledge in **liver transplant** patients after pharmacy counseling]. Evaluation de l'apport d'une consultation de pharmacie sur les connaissances des patients transplantes hepatiques.

L2 ANSWER 22 OF 85 MEDLINE on STN
TI Adenovirus infection in pediatric small bowel transplantation recipients.

L2 ANSWER 23 OF 85 MEDLINE on STN
TI Transplantation of the abdominal wall.

L2 ANSWER 24 OF 85 MEDLINE on STN
TI Insulin-like growth factor-I enhances choleretic action of FK506 in rats.

L2 ANSWER 25 OF 85 MEDLINE on STN
TI The effect of immunosuppressive regimens on the recurrence of primary biliary cirrhosis after **liver** transplantation.

L2 ANSWER 26 OF 85 MEDLINE on STN
TI Different immunosuppressive regimens and recurrence of primary sclerosing cholangitis after **liver** transplantation.

L2 ANSWER 27 OF 85 MEDLINE on STN
TI Tacrolimus: a further update of its use in the management of organ transplantation.

L2 ANSWER 28 OF 85 MEDLINE on STN
TI Early steroid withdrawal after **liver** transplantation: the Canadian tacrolimus versus microemulsion cyclosporin A trial: 1-year follow-up.

L2 ANSWER 29 OF 85 MEDLINE on STN
TI Toward better outcomes with tacrolimus therapy: population pharmacokinetics and individualized dosage prediction in adult **liver** transplantation.

L2 ANSWER 30 OF 85 MEDLINE on STN
TI Therapy for acute rejection in pediatric organ **transplant** recipients.

L2 ANSWER 31 OF 85 MEDLINE on STN
TI Population pharmacokinetics of tacrolimus in adult kidney **transplant** recipients.

L2 ANSWER 32 OF 85 MEDLINE on STN
TI Comparison of two population pharmacokinetic programs, NONMEM and P-PHARM, for tacrolimus.

L2 ANSWER 33 OF 85 MEDLINE on STN

MMP-13 inhibitors

TI A 38-year-old African-American woman with an unusually rapid progression of "Primary Biliary Cirrhosis": a missed opportunity!.

L2 ANSWER 34 OF 85 MEDLINE on STN
TI Chronic graft-versus-host disease and late effects after hematopoietic stem cell transplantation.

L2 ANSWER 35 OF 85 MEDLINE on STN
TI Orthotopic **liver** transplantation for acute **liver** failure secondary to autoimmune hepatitis in a child with autoimmune polyglandular syndrome type 1.

L2 ANSWER 36 OF 85 MEDLINE on STN
TI Growth following solid-organ transplantation.

L2 ANSWER 37 OF 85 MEDLINE on STN
TI Steroid elimination 24 hours after **liver** transplantation using daclizumab, tacrolimus, and mycophenolate mofetil.

L2 ANSWER 38 OF 85 MEDLINE on STN
TI Vertebral morphometry by X-ray absorptiometry before and after **liver transplant**: a cross-sectional study.

L2 ANSWER 39 OF 85 MEDLINE on STN
TI Cyclosporin: an updated review of the pharmacokinetic properties, clinical efficacy and tolerability of a microemulsion-based formulation (neoral)1 in organ transplantation.

L2 ANSWER 40 OF 85 MEDLINE on STN
TI Daclizumab: a review of its use in the management of organ transplantation.

=> s l2 and py<2001
12889759 PY<2001
(PY<20010000)
L6 40 L2 AND PY<2001

=> d L6 1-40 ti

L6 ANSWER 1 OF 40 MEDLINE on STN
TI [Infection after orthotopic **liver** transplantation: analysis of the first 120 consecutive cases].
Infeccion despues del trasplante hepatico ortotopico: analisis de los 120 primeros casos consecutivos.

L6 ANSWER 2 OF 40 MEDLINE on STN
TI Transplantation osteoporosis and **corticosteroid**-induced osteoporosis in autoimmune diseases: experience with alfacalcidol.

L6 ANSWER 3 OF 40 MEDLINE on STN
TI Tacrolimus: a further update of its pharmacology and therapeutic use in the management of organ transplantation.

L6 ANSWER 4 OF 40 MEDLINE on STN
TI Evidence that apoptosis of activated T cells occurs in spontaneous tolerance of **liver** allografts and is blocked by manipulations which break tolerance.

L6 ANSWER 5 OF 40 MEDLINE on STN
TI A prospective study of hepatitis C viremia in renal allograft recipients.

MMP-13 inhibitors

L6 ANSWER 6 OF 40 MEDLINE on STN
TI Linear growth after pediatric **liver** transplantation.

L6 ANSWER 7 OF 40 MEDLINE on STN
TI Effects of corticosteroids on HCV infection.

L6 ANSWER 8 OF 40 MEDLINE on STN
TI Steroid therapy in fulminant hepatic failure secondary to autoimmune hepatitis.

L6 ANSWER 9 OF 40 MEDLINE on STN
TI Therapeutic drug monitoring of tacrolimus in **liver** transplantation, phase III FK506 multicenter Spanish Study Group: a two-year follow-up.

L6 ANSWER 10 OF 40 MEDLINE on STN
TI Lymphocytic gastritis resembling graft-vs.-host disease following autologous hematopoietic cell transplantation.

L6 ANSWER 11 OF 40 MEDLINE on STN
TI Influence of posttransplant time on dose and concentration of tacrolimus in **liver transplant** patients.

L6 ANSWER 12 OF 40 MEDLINE on STN
TI Lipoprotein abnormalities in long-term stable **liver** and renal transplanted patients. A comparative study.

L6 ANSWER 13 OF 40 MEDLINE on STN
TI Causes of leukocytosis in **liver transplant** recipients: relevance in clinical practice.

L6 ANSWER 14 OF 40 MEDLINE on STN
TI Interferon-alpha for prophylaxis of recurrent viral hepatitis C in **liver transplant** recipients: a prospective, randomized, controlled trial.

L6 ANSWER 15 OF 40 MEDLINE on STN
TI Posttransplant eosinophilic gastroenteritis in children.

L6 ANSWER 16 OF 40 MEDLINE on STN
TI Hepatic allograft rejection is associated with increased levels of soluble intercellular adhesion molecule-1.

L6 ANSWER 17 OF 40 MEDLINE on STN
TI Risk factors for premature coronary heart disease after successful **liver** transplantation in adults.

L6 ANSWER 18 OF 40 MEDLINE on STN
TI Post-**transplant** diabetes mellitus. The role of immunosuppression.

L6 ANSWER 19 OF 40 MEDLINE on STN
TI Phase I trial of cyclosporine-induced autologous graft-versus-host disease in patients with multiple myeloma undergoing high-dose chemotherapy with autologous stem-cell rescue.

L6 ANSWER 20 OF 40 MEDLINE on STN
TI Transplantation for fulminant hepatic failure: comparing tacrolimus versus cyclosporine for immunosuppression and the outcome in elective transplants. European FK506 **Liver** Study Group.

L6 ANSWER 21 OF 40 MEDLINE on STN

MMP-13 inhibitors

TI FK 506 therapy for refractory renal allograft rejection: lessons from **liver** transplantation.

L6 ANSWER 22 OF 40 MEDLINE on STN
TI Corticosteroids and ulcers: is there an association?.

L6 ANSWER 23 OF 40 MEDLINE on STN
TI The side effect profile of sirolimus: a phase I study in quiescent cyclosporine-prednisone-treated renal **transplant** patients.

L6 ANSWER 24 OF 40 MEDLINE on STN
TI Increased infections in **liver transplant** recipients with recurrent hepatitis C virus hepatitis.

L6 ANSWER 25 OF 40 MEDLINE on STN
TI Hepatic expression of macrophage inflammatory protein-1 alpha and macrophage inflammatory protein-1 beta after **liver** transplantation.

L6 ANSWER 26 OF 40 MEDLINE on STN
TI **Corticosteroid** withdrawal after **liver** transplantation.

L6 ANSWER 27 OF 40 MEDLINE on STN
TI Histological and biochemical effects of cyclosporine A withdrawal from a triple drug regimen after over 2 years of treatment in **liver transplant** patients.

L6 ANSWER 28 OF 40 MEDLINE on STN
TI Patients with chronic hepatitis--potential risks when undergoing dental surgery: review and case report.

L6 ANSWER 29 OF 40 MEDLINE on STN
TI Glucose homeostasis during exercise in humans with a **liver** or kidney **transplant**.

L6 ANSWER 30 OF 40 MEDLINE on STN
TI FK506 (tacrolimus) compared with cyclosporine for primary immunosuppression after pediatric **liver** transplantation. Results from the U.S. Multicenter Trial.

L6 ANSWER 31 OF 40 MEDLINE on STN
TI A comparison of tacrolimus (FK 506) and cyclosporine for immunosuppression in **liver** transplantation. The U.S. Multicenter FK506 **Liver** Study Group.

L6 ANSWER 32 OF 40 MEDLINE on STN
TI Randomised trial comparing tacrolimus (FK506) and cyclosporin in prevention of **liver** allograft rejection. European FK506 Multicentre **Liver** Study Group.

L6 ANSWER 33 OF 40 MEDLINE on STN
TI Cyclophosphamide as an alternative to azathioprine in cardiac **transplant** recipients with suspected azathioprine-induced hepatotoxicity.

L6 ANSWER 34 OF 40 MEDLINE on STN
TI The use of mycophenolate mofetil (RS-61443) in human heart **transplant** recipients.

L6 ANSWER 35 OF 40 MEDLINE on STN
TI Muromonab CD-3: a review of its pharmacology, pharmacokinetics, and clinical use in transplantation.

L6 ANSWER 36 OF 40 MEDLINE on STN
TI Monitoring of bone marrow **transplant** recipient **liver** by fine-needle aspiration biopsy.

L6 ANSWER 37 OF 40 MEDLINE on STN
TI Steroid-responsive chronic hepatic graft-versus-host disease without extrahepatic graft-versus-host disease.

L6 ANSWER 38 OF 40 MEDLINE on STN
TI Prophylaxis with ranitidine against peptic ulcer disease after **liver** transplantation.

L6 ANSWER 39 OF 40 MEDLINE on STN
TI Survival following hepatic transplantation in the cyclosporine era.

L6 ANSWER 40 OF 40 MEDLINE on STN
TI Varicella in children with renal transplants.

=> d L6 26 ti abs bib

L6 ANSWER 26 OF 40 MEDLINE on STN
TI **Corticosteroid** withdrawal after **liver** transplantation.
AB BACKGROUND. Long-term side effects of corticosteroids (CSs) result in > major morbidity for recipients of orthotopic **liver** transplants (OLT). We instituted a program of CS withdrawal among OLT recipients to quantify the contribution of CS to adverse clinical sequelae and to determine whether long-term CS administration is necessary to avoid rejection. METHODS. Recipients who had normal allograft function on CS, cyclosporine, and azathioprine more than 1 year after OLT were offered CS withdrawal during 12 to 22 weeks. Patients underwent routine clinical monitoring and laboratory studies. Continuous variables were compared by paired t test analysis. RESULTS. CSs were discontinued in 51 recipients; 45 (88%) of 51 patients remain steroid-free after a mean follow-up of 13.8 months (range, 4 to 36). CS therapy was reinstituted in 6 patients who had abnormal transaminase levels during routine follow-up. Among the patients who remain off CS, there were no significant changes in blood pressure, transaminase, alkaline phosphatase, bilirubin, or glucose levels during the study period. Mean number of blood pressure medications decreased from 0.7 +/- 0.1 to 0.4 +/- 0.1 ($p = 0.007$). Cholesterol decreased from 217 +/- 8 mg/dl on CS to 204 +/- 9 mg/dl at 1 month ($p = 0.0001$), 183 +/- 10 mg/dl at 3 months ($p = 0.0001$), 198 +/- 8 mg/dl at 6 months ($p = 0.04$), 213 +/- 11 mg/dl at 12 months ($p = 0.01$), 209 mg/dl +/- 16 at 18 months ($p = 0.02$), and 183 +/- 19 mg/dl at 24 months ($p = 0.2$) off CS. Weight loss occurred in 88% of patients and averaged 9.5 pounds. CONCLUSIONS. CS therapy can be successfully withdrawn without precipitating rejection in **liver transplant** recipients who have stable graft function 1 year after OLT. The incidence and severity of hypertension and hypercholesterolemia are reduced in patients whose CSs have been withdrawn.
AN 96006387 MEDLINE
DN PubMed ID: 7570337
TI **Corticosteroid** withdrawal after **liver** transplantation.
AU Punch J D; Shieck V L; Campbell D A; Bromberg J S; Turcotte J G; Merion R M
CS Department of Surgery, University of Michigan Medical School, Ann Arbor, USA.
SO Surgery, **(1995 Oct)** Vol. 118, No. 4, pp. 783-6; discussion 786-8.
Journal code: 0417347. ISSN: 0039-6060.
CY United States

MMP-13 inhibitors

DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199511
ED Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951107

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.00	5.21

FILE 'STNGUIDE' ENTERED AT 13:52:30 ON 13 APR 2006

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 7, 2006 (20060407/UP).

=> d L6 39 ti abs bib
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE' - CONTINUE? (Y)/N:y

L6 ANSWER 39 OF 40 MEDLINE on STN
TI Survival following hepatic transplantation in the cyclosporine era.
AB In a series of 50 consecutive patients receiving 55 hepatic transplants, the 6-month survival was 76 per cent. Mortality was considerably higher in patients with complications of advanced **liver** failure (56%) than in patients that were not hospital-confined preceding the **transplant** procedure (10%). The causes of death were related primarily to technical errors, and uncommonly caused by rejection or uncontrollable infection. This striking change in the cause of death occurring in the cyclosporine era results from the use of more specific immunosuppression and close scrutiny of the allograft with frequent hepatic biopsy. Both of these principles diminish the reliance on high-dose **corticosteroid** therapy, and therefore promote wound healing and resistance to fatal infection.
AN 86240454 MEDLINE
DN PubMed ID: 3521421
TI Survival following hepatic transplantation in the cyclosporine era.
AU Williams J W; Vera S R; Peters T G; Van Voorst S
SO The American surgeon, **(1986 Jun)** Vol. 52, No. 6, pp. 291-3.
Journal code: 0370522. ISSN: 0003-1348.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198607
ED Entered STN: 19900321
Last Updated on STN: 19980206
Entered Medline: 19860708

10613788

STN Search from parent case

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=> d his
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     FILE 'EUROPATFULL, PCTFULL, USPATFULL' ENTERED AT 14:19:44 ON 27 JUN 2001
                E MCDONALD GEORGE/IN
L1            40 S E3-E12
L2            14 S E3-E4

     FILE 'PCTFULL' ENTERED AT 14:25:28 ON 27 JUN 2001
L3            12 S DRUG RESEARCH/PA
L4          3845 S CORTICOSTEROID# OR BECLOMETHASONE#

     FILE 'EUROPATFULL, PCTFULL, USPATFULL' ENTERED AT 14:27:34 ON 27 JUN 2001
L5             1 S L3(L)L4

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 14:33:21 ON 27 JUN 2001
L6            57 S MCDONALD GEORGE B/AU
L7        186255 S L4
L8             0 S L7(L)L6
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L6 ANSWER 12 OF 57 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:464054 CAPLUS
DOCUMENT NUMBER: 125:158046
TITLE: Evaluation of a CD5-specific immunotoxin for treatment of acute graft-versus-host disease after allogeneic marrow transplantation
AUTHOR(S): Martin, Paul J.; Nelson, Betty J.; Appelbaum, Frederick R.; Anasetti, Claudio; Deeg, H. Joachim; Hansen, John A.; **McDonald, George B.**; Nach, Richard A.; Sullivan, Kehti M.; et al.
CORPORATE SOURCE: Fred Hutchinson Cancer Res. Cent., Seattle, WA, 98104, USA
SOURCE: Blood (1996), 88(3), 824-830
CODEN: BLOOAW; ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Acute graft-vs.-host disease (GVHD) is most often treated with high dose glucocorticoids, but less than half to patients have durable overall improvement. Previous phase I and phase II studies suggested that treatment with CD5-specific immunotoxin (XomaZyme-CD5 Plus) could ameliorate symptoms of GVHD. In a randomized, double-blind trial, we compared ZomaZyme-CD5 Plus and glucocorticoids vs. placebo and glucocorticoids as initial therapy for 243 patients who developed acute GVHD after allogeneic marrow transplantation. The study drug (XomaZyme CD5-Plus or an identical appearing placebo) was administered at a dose of 0.1 mg/kg body wt. on each of 14 consecutive days. All patients were treated concomitantly with a std. regimen of methylprednisolone. At the time of entry on study, 94% of patients had a rash, 56% had hyperbilirubinemia, 61% had diarrhea, and 84% had nausea and vomiting. At 3, 4, and 5 wks. after starting treatment, symptom severity was less in the CD5 group than in the placebo group. At 4 wks., 40% of patients assigned to the CD5 group had complete response compared with 25% of these assigned to the control group. At 6 wks., 44% of patients assigned to CD5 group had complete response as compared with 38% in the placebo group. Clin. extensive chronic GVHD developed in 65% of patients in the CD5 group compared with 72% in the control group. Survival at 1 y after treatment was 49% in the CD5 group and 45% in the control group. Side effects required close monitoring and appropriate adjustment of treatment. The combined administration of a CD5-specific immunotoxin and glucocorticoids controls GVHD manifestations more effectively than treatment with glucocorticoids alone during the first 5 wks. after starting treatment. Use of this immunotoxin does not result in any long-term clin. benefit for patients with acute GVHD.

L6 ANSWER 13 OF 57 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:49517 CAPLUS
DOCUMENT NUMBER: 124:165529
TITLE: Oral beclomethasone dipropionate for treatment of human intestinal graft-versus-host disease
AUTHOR(S): Baehr, Paul H.; Levine, Douglas S.; Bouvier, Michelle E.; Hockenbery, David M.; Gooley, Ted A.; Stern, Jean

G.; Martin, Paul J.; **McDonald, George B.**
CORPORATE SOURCE: Clinical Research Division of the Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA, USA
SOURCE: Transplantation (1995), 60(11), 1231-8
CODEN: TRPLAU; ISSN: 0041-1337
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oral beclomethasone dipropionate (BDP), a potent, topically active corticosteroid, was investigated as therapy for the title disease. Allogeneic marrow-graft recipients with biopsy-proven intestinal graft-vs.-host disease of mild-to-moderate severity received BDP (8 mg daily) for .ltoreq.28 days. Improvement was seen in appetite, oral food intake, nausea, and diarrhea over the course of therapy, and an overall beneficial response was obsd. in 72% of 40 evaluable patients. Surveillance cultures of throat and stools showed no increase in bacterial or fungal colonization over time. The adrenal axis became suppressed in 11 of 20 evaluable patients (55%) but suppression was not a prerequisite for clin. response, as 6 of 9 patients who retained normal adrenal function improved clin. It is concluded that oral BDP is a safe and effective treatment for mild-to-moderate intestinal graft-vs.-host disease. Systemic absorption probably occurs, but adrenal suppression is not a prerequisite for clin. efficacy, suggesting that the biol. effect is primarily topical.

L6 ANSWER 35 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:352139 BIOSIS
DOCUMENT NUMBER: PREV199800352139
TITLE: Oral beclomethasone dipropionate for treatment of intestinal graft-versus-host disease: A randomized, controlled trial.
AUTHOR(S): **McDonald, George B. (1)**; Bouver, Michelle; Hockenbery, David M.; Stern, Jean M.; Gooley, Ted; Farrand, Allen; Murakami, Carol; Levine, Douglas S.
CORPORATE SOURCE: (1) Gastroenterol./Hepatol. Section, Ferd Hutchinson Cancer Res. Cent., 1100 Fairview Ave. N., P.O. Box 19024, Seattle, WA 98109-1024 USA
SOURCE: Gastroenterology, (July, 1998) Vol. 115, No. 1, pp. 28-35.
ISSN: 0016-5085.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Background & Aims: Beclomethasone dipropionate (BDP), a topically active steroid, seemed to be an effective treatment for intestinal graft-versus-host disease (GVHD) in a phase I study. The aim of this study was to compare the effectiveness of oral BDP to that of placebo capsules in treatment of intestinal GVHD. Methods: Sixty patients with anorexia and poor oral intake because of intestinal GVHD were randomized to receive prednisone (1 mg cntdot kg-1 cntdot day-1) plus either oral BDP (8 mg/day) or placebo capsules. Initial responders who were eating at least 70% of

caloric needs at evaluation on day 10 continued to take study capsules for an additional 20 days while the prednisone dose was rapidly tapered. The primary end point was the frequency of a durable treatment response at day 30 of treatment. Results: The initial treatment response at day 10 was 22 of 31 (71%) in the BDP/prednisone group vs. 16 of 29 (55%) for the placebo/prednisone group. The durable treatment response at day 30 was 22 of 31 (71%) vs. 12 of 29 (41%), respectively (P = 0.02). Conclusions: The combination of oral BDP capsules and prednisone was more effective than prednisone alone in treating intestinal GVHD. Oral BDP allowed prednisone doses to be rapidly tapered without recurrent intestinal symptoms.

L6 ANSWER 42 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:66300 BIOSIS
DOCUMENT NUMBER: PREV199698638435
TITLE: Oral beclomethasone dipropionate for treatment of human intestinal graft-versus-host disease.
AUTHOR(S): Baehr, Paul H.; Levine, Douglas S.; Bouvier, Michelle E.; Hockenbery, David M.; Gooley, Ted A.; Stern, Jean G.; Martin, Paul J.; **McDonald, George B.**
CORPORATE SOURCE: Gastroenterology/Hepatology Sect., Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA 98104 USA
SOURCE: Transplantation (Baltimore), (1995) Vol. 60, No. 11, pp. 1231-1238.
ISSN: 0041-1337.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Intestinal graft-versus-host disease (GVHD) causes anorexia, vomiting, abdominal pain, and diarrhea. We investigated oral beclomethasone dipropionate (BDP), a potent, topically active corticosteroid, as therapy for this disease. Forty-two allogeneic marrow-graft recipients with biopsy-proven intestinal graft-versus-host disease of mild-to-moderate severity received BDP (8 mg daily) for up to 28 days. Weekly symptom scores, oral intake, and surveillance throat and stool cultures were compared with baseline values. Adrenal testing was performed serially in patients not receiving concurrent prednisone. Improvement was seen in appetite (P lt 0.001), oral intake (P lt 0.001), nausea (P=0.013), and diarrhea (P=0.02) over the course of therapy, and an overall beneficial response was observed in 72% of 40 evaluable patients. Surveillance cultures of throat and stool showed no increase in bacterial or fungal colonization over time. The adrenal axis became suppressed in 11 of 20 evaluable patients (55%) but suppression was not a prerequisite for clinical response, as 6 of 9 patients who retained normal adrenal function improved clinically. We conclude that oral BDP is a safe and effective treatment for mild-to-moderate intestinal graft-versus-host disease. Systemic absorption probably occurs, but adrenal suppression is not a prerequisite for clinical efficacy, suggesting that the biological effect is primarily topical. BDP should be further investigated as a topical therapy for intestinal GVHD.

L6 ANSWER 12 OF 57 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:464054 CAPLUS
DOCUMENT NUMBER: 125:158046
TITLE: Evaluation of a CD5-specific immunotoxin for treatment of acute graft-versus-host disease after allogeneic

marrow transplantation
AUTHOR(S): Martin, Paul J.; Nelson, Betty J.; Appelbaum, Frederick R.; Anasetti, Claudio; Deeg, H. Joachim; Hansen, John A.; **McDonald, George B.**; Nach, Richard A.; Sullivan, Kehti M.; et al.
CORPORATE SOURCE: Fred Hutchinson Cancer Res. Cent., Seattle, WA, 98104,
USA
SOURCE: Blood (1996), 88(3), 824-830
CODEN: BLOOAW; ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Acute graft-vs.-host disease (GVHD) is most often treated with high dose glucocorticoids, but less than half to patients have durable overall improvement. Previous phase I and phase II studies suggested that treatment with CD5-specific immunotoxin (XomaZyme-CD5 Plus) could ameliorate symptoms of GVHD. In a randomized, double-blind trial, we compared ZomaZyme-CD5 Plus and glucocorticoids vs. placebo and glucocorticoids as initial therapy for 243 patients who developed acute GVHD after allogeneic marrow transplantation. The study drug (XomaZyme CD5-Plus or an identical appearing placebo) was administered at a dose of 0.1 mg/kg body wt. on each of 14 consecutive days. All patients were treated concomitantly with a std. regimen of methylprednisolone. At the time of entry on study, 94% of patients had a rash, 56% had hyperbilirubinemia, 61% had diarrhea, and 84% had nausea and vomiting. At 3, 4, and 5 wks. after starting treatment, symptom severity was less in the CD5 group than in the placebo group. At 4 wks., 40% of patients assigned to the CD5 group had complete response compared with 25% of these assigned to the control group. At 6 wks., 44% of patients assigned to CD5 group had complete response as compared with 38% in the placebo group. Clin. extensive chronic GVHD developed in 65% of patients in the CD5 group compared with 72% in the control group. Survival at 1 y after treatment was 49% in the CD5 group and 45% in the control group. Side effects required close monitoring and appropriate adjustment of treatment. The combined administration of a CD5-specific immunotoxin and glucocorticoids controls GVHD manifestations more effectively than treatment with glucocorticoids alone during the first 5 wks. after starting treatment. Use of this immunotoxin does not result in any long-term clin. benefit for patients with acute GVHD.

L6 ANSWER 23 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:52813 BIOSIS
DOCUMENT NUMBER: PREV200100052813
TITLE: Chronic graft-versus-host disease of the liver: Presentation as an acute hepatitis.
AUTHOR(S): Strasser, Simone I.; Shulman, Howard M.; Flowers, Mary E.; Reddy, Rajender; Margolis, David A.; Prumbaum, Manfred; Seropian, Stuart E.; **McDonald, George B. (1)**
CORPORATE SOURCE: (1) Gastroenterology/Hepatology Section, Fred Hutchinson Cancer Research Center, 1100 Fairview Ave N., D2-190, Seattle, WA, 98109-1024 USA
SOURCE: Hepatology, (December, 2000) Vol. 32, No. 6, pp. 1265-1271.